



# Thinking about Ginkgo?

Think again. A new study finds ginkgo biloba does not prevent Alzheimer's.

BY DAN HURLEY

**T**he latest study to find that the popular herbal product ginkgo biloba does not prevent or slow Alzheimer's disease is raising new questions about why so many people continue to take it.

Along with fish oil and vitamin E, ginkgo is widely marketed as a "natural" way for older adults to stay sharp and avoid the ravages of dementia. But while all three supplements showed signs of possible benefit in early studies, larger and more carefully designed studies have failed to confirm the initial promise. In the meanwhile, concerns have grown about potential side effects.

By far the largest and longest study of its kind, the Ginkgo Evaluation of Memory (GEM) study involved over 3,000 adults aged 75 and up who took ginkgo or a placebo for just over six years. It was funded by the National Institutes of Health, conducted at five sites across the United States, and led by Steven T. DeKosky, M.D., dean of the School of Medicine at the University of Virginia in Charlottesville.

The GEM study found no benefit from ginkgo in slowing the risk of developing dementia or Alzheimer's. In fact, the group given ginkgo actually had a 12 percent increased risk of developing dementia and a 16 percent increased risk of developing Alzheimer's, although the differences were not large enough to be statistically significant.

"Users of this extract should not expect it to be helpful," stated an editorial accompanying the study in the November 18, 2008, edition of the *Journal of the American Medical Association*. The editorial, by Lon S. Schneider, M.D., professor of psychiatry, neurology, and gerontology at the University of Southern California's Keck School of Medicine, noted that the new results must be considered in the context of many other studies that have shown equally disappointing results.

"The GEM study adds to the substantial body of evidence that ginkgo biloba extract



A leaf from the ginkgo tree.  
Has ginkgo's early promise faded?

as it is generally used does not prevent dementia in individuals with or without cognitive impairment and is not effective for Alzheimer disease," Dr. Schneider wrote.

Moreover, the study found that eight patients taking ginkgo suffered a so-called "hemorrhagic" stroke caused by bleeding in the brain, compared to four taking the placebo. Although the differences were not statistically significant, ginkgo has long been known to increase the risk of bleeding due to its blood-thinning effects. Ginkgo was recently cited in another study as among the most common and potentially severe causes of harmful drug-supplement interactions when taken with aspirin.

The only criticism of the study came from herbal industry trade associations. "The study does not in any way undermine what has already been observed," said Michael McGuffin, president of the American Herbal Products Association.

## WHY WE BELIEVE AND BUY

Along with other recent evidence of ginkgo's ineffectiveness, the new study could mark the end of the line for serious studies of the product, but it probably will not deter the supplement industry from continuing to pitch it, says David Knopman M.D., professor of neurology at the Mayo Clinic in Rochester, MN.

"It is amazing to me how people are willing to take these things with so little genuine proof that they work, when they are so skeptical about prescription medications that have undergone years of careful testing," Dr. Knopman says.

According to the 2007 National Health Interview Survey, ginkgo is one of the top 10 natural products used by Americans. Annual sales in the U.S. were estimated at over \$249 million in 2006.

One reason that consumers continue to seek out such products, according to Dr. Knopman, is that the handful of drugs

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approved by the Food and Drug Administration for the treatment of dementia have only a modest and temporary benefit.

"When there's an absence of a good therapy," Dr. Knopman notes, "people grasp at straws." For instance, the National Institute of Aging notes that the benefit of memantine (Namenda) may be as minimal as extending for just a few months the ability of a person with advanced Alzheimer's to use a bathroom independently. Dr. Knopman emphasizes, however, that at least with FDA-approved drugs like memantine and donepezil (Aricept), the benefits—while modest—have been carefully established in well-designed studies involving thousands of patients.

Another reason for Americans' continued enthusiasm for ginkgo and other supplements is that companies selling them do not require the approval of the FDA, and are legally permitted to market them with vague claims of benefit so long as they do not plainly assert that they cure, treat, or prevent any illness. As a result, even major pharmaceutical companies have gotten into the game of selling supplements. Bayer, for instance, now markets formulations of its "One A Day" brand to men and women over 50 that contain ginkgo "to promote memory and concentration," according to the label.

#### OTHER SUPPLEMENTS

While the new study may close the book on ginkgo—at least from a scientific point of view—the picture remains murkier for vitamin E and fish oil as possible treatments or preventive therapies for dementia.

According to John Hart, Jr., M.D., medical science director of the Center for Brain Health at the University of Texas at Dallas, the scientific picture on vitamin E and fish oil (and the omega-3 fatty acids found within fish oil) remains where ginkgo was before the GEM study. That is, early studies that looked promising have not been

borne out by later, more carefully conducted studies, but there has yet to be a study as large and definitive as GEM to settle the matter one way or the other.

"Without a landmark study on omega-3 fatty acids, we can't be sure," Dr. Hart says. "But anything that improves the circulation, as omega-3 fatty acids appear to do, should help the brain."

In August 2008, researchers from the Netherlands published a long-awaited study in the journal *Neurology* finding no benefit on mental performance for omega-3 fatty acids compared to placebo after 26 weeks of treatment in 302 people aged 70 and older. That study drew particular interest because it was designed to test the supplement as a preventive strategy in seniors who had no signs of dementia or Alzheimer's disease before the treatment began.

Another study, published in the *Archives of Neurology* in October of 2006, involved 204 people with mild to moderate Alzheimer's who were given either omega-3 fatty acids or a placebo for six months. As a group the mental status of patients taking omega-3 fatty acids declined just as quickly as those taking placebo, although those with the mildest symptoms (at least 27 on a 30-point scale of mental status, where 30 is normal) at the beginning of the study did fade more slowly. These patients declined only by about one point after 12 months if they took omega-3, compared to about three points if they took a placebo—a statistically significant difference.

What about vitamin E? In 2005, the *New England Journal of Medicine* published the results of a three-year study in 769 people with mild cognitive impairment, a condition in which memory and thinking are not yet severely disabled. Those who took vitamin E declined just as quickly as those who took a placebo, the study found.

Another study, of 155 people who already had Alzheimer's but were still well enough to live at home, found that over the course of two years, 55 percent of those taking vitamin E experienced a significant decline, compared to 74 percent of those taking a placebo. But three times as many of those taking vitamin E suffered a fall. And other studies, designed to test the use of vitamin E to prevent heart attacks and strokes, have found that it either has no benefit or actually increases the risk somewhat. Just last year, for instance, an eight-year study by Harvard researchers involving 14,641 men found that taking 400 IU of vitamin E every other day increased their risk of stroke caused by bleeding in the brain by 74 percent, a significant difference. As a result of such concerns, the American Heart Association recommends against the use of vitamin E supplements.

Dr. Hart urges caution with vitamin E. "I haven't been recommending it," he says.

Still, hope springs eternal for finding an effective herb for preventing or treating Alzheimer's. Studies are underway, funded by the National Center for Complementary and Alternative Medicine, investigating the effects of everything from antioxidants in grapes to such a commercial product called TeaMem.

Meanwhile, Dr. Hart recommends that people concerned about the effects of aging on their brains stick to the basics: diet, exercise, and no smoking. "The other thing I'm really big on," Dr. Hart says, "is controlling high blood pressure, diabetes, and cholesterol. It appears that reducing and treating those risk factors are really important for the prevention of Alzheimer's."

They might not be as alluring and simple as popping an inexpensive pill that's touted as safe and natural, but they have one thing going for them, Dr. Hart says: "They have been proven to work." NN